UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,248	03/07/2000	Sergio Abgrignani	CHIR-0234	9892

27476 7590 07/02/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/520,248	ABGRIGNANI, SERGIO	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3-6,10 and 11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3-6,10,11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/776259.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 1,3-6,10,11 are under consideration.

2. The previously pending rejections are withdrawn in view of the amended claims.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 5 and 6 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 5 and 6 are indefinite in that it is unclear to what the recited dosages refer. The addition of "contacted with the cells" to said claim does not clarify this issue. It is unclear whether said dosage refers to a dosage of 100U/ml of IL-2 wherein the concentration refers to concentration of IL-2 in the dose administered to a subject, or whether it refers to the concentration of IL-2 in the blood or tissue fluid following administration and distribution into these compartments or what said dosage means. It is also unclear as to what "contacted with the cells" means in the context recited in the claim. Regarding applicants previous comments, the specification, page 10, lines 11-25 refers to an in vitro experiment. It provides no explanation as to what the dosage recited in the claims means in the context of in vivo administration. There is no disclosure in the specification as to what the dosage recited in the claims means in the context of an in vivo method and said dosage has no art recognized meaning in the context of an in vivo method. The specification, page 3 also does not clarify what this means. Based on the specification, page 10, it appears that the limitation as disclosed in page 3 of the specification actually refers to a concentration for in vitro use, but this is not specifically stated in the specification.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "contacted with the cells" in claim 5 or 6. Said phrase is not found in the specification as originally filed. The specification, page 10, discloses the addition of the cytokines recited in the claims in concentrations encompassed in the claims wherein the cytokines are added *in vitro* to cells in a microtiter plate. However, there is no disclosure in the specification as originally filed that the dosages disclosed in page 3 of the specification are used to "contact cells" in vivo. The claims encompass a method of use in vivo. There is no disclosure in the specification as to what the particular dosages disclosed in the specification actually refer. As per above, it is also unclear as to what the aforementioned dosages refers to in the context of an in vivo method and it is also unclear as to what "contacted with the cells" means in the context recited in the claims. There is no support in the specification as originally filed for the claimed invention (eg. the claimed invention constitutes new matter).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1,3-6,10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al. (U.S. Patent 5,425,940) in view of Clark et al.

Zimmerman et al. disclose in vivo administration of a combination of IL-2 and TNF-alpha (AKA TNF, wherein lymphotoxin is known in the art as TNF-beta) for treatment of tumors (see abstract). The combination of IL-2 and TNF-alpha are administered independent of antigen (they are administered without administration of antigen). The method results in antigen independent activation of T cells because the

method has the same steps as the originally claimed method. The cells recited in claims 3 and 4 are present in vivo in humans (as are all possible types of immune cells which would be present in any individual in the absence of a specific genetic defect that would result in the absence of a particular cell population). Zimmerman et al. does not disclose the use of IL-6 with IL-2 and TNF. Clark et al. disclose that IL-6 can be used in cancer therapy (see abstract and column 6, second complete paragraph). Clark et al. disclose that IL-6 can be used in combination with other therapeutic agents (see column 5, third paragraph). Clark et al. disclose that IL-6 can be used in combination with IL-2 for cancer therapy (see column 6, fifth paragraph). The combination of IL-2 and IL-6 are administered independent of antigen (they are administered without administration of antigen). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Zimmerman et al. disclose administration of a combination of IL-2 and TNF-alpha for treatment of tumors whilst Clark et al. disclose that IL-6 can be used in combination with IL-2 for cancer therapy. One of ordinary skill in the art would have been motivated to do the aforementioned because Clark et al. disclose that IL-6 can be used in combination with other therapeutic agents and that IL-6 can be used in combination with IL-2 for cancer therapy, whilst Zimmerman et al. disclose the advantages of using TNF and IL-2 for treating cancer (see abstract). The particular dosages recited in claims 5 and 6 would have determined by routine experimentation (while the dosages recited in the claim are indefinite for the reasons stated above, for the purpose of the prior art it will be assumed that they encompass a working embodiment of the claimed method).

Regarding applicants comments about synergistic effect as per the specification, page 12, said passage of the specification refers to an in vitro assay using particular cells examined under particular conditions, wherein the claimed invention is drawn to an in vivo method of treatment. Therefore, the aforementioned teaching is not germane to the claimed invention.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached Monday through Thursday from 7:30am to 6:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644